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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
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☐ *Additional inventors are being named on the ____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (280 characters max)

PROCESS AND MACHINE FOR AUTOMATED MANUFACTURE OF COVERED RETARD FORMS

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 23 ☐ CD(s), Number

☒ Drawing(s) *Number of Sheets* 26 ☐ Other (specify)

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

		FILING FEE AMOUNT ($)
☐	Applicant claims small entity status. See 37 CFR 1.27.	
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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.

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Respectfully submitted,

SIGNATURE Gary Hecht

Date 07-30-2003

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REGISTRATION NO. *(if appropriate)* 36,826

Docket Number: 26591 USA

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USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C.

CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10) Applicant(s): J. M odley			Docket No. 26591 USA
Serial No. N/A	Filing Date Herewith	Examiner N/A	Group Art Unit N/A

Invention: **PROCESS AND MACHINE FOR AUTOMATED MANUFACTURE OF COVERED RETARD FORMS**

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Provisional Patent Application
Docket No. P-26591 USA

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PROCESS AND MACHINE FOR AUTOMATED MANUFACTURE OF COVERED RETARD FORMS

Background

The present invention relates to a process and an apparatus for the automated manufacture of a gastro-retentive drug delivery device, and more particularly to the automated manufacture of a covered retard form such as that disclosed in U.S. Patent No. 4,996,058, which is hereby incorporated herein by reference.

The term "retard form" denotes a dosage form which effects delayed release of the active ingredient in the stomach and to the upper part of the small intestine in comparison with conventional dosage forms, such as customary tablets or capsules. Avoiding an undesirably high initial dose, the release is effected continuously over a relatively long period and controlled at a therapeutically effective level. The subject retard form is orally administered and, once in contact with the stomach fluids, expands so as to float on the stomach fluids and/or be retained within the space of the stomach due to its size following inflation, which precludes passage across the pylorus sphincter. In this manner it remains in the stomach to insure continuous controlled release of the physiologically active ingredients.

The subject retard form is characterized preferably, at least in one form, by the following:

(a) at least one component that expands on contact with body fluid and which contains a substance that generates a blowing agent, a physiologically active substance or a

combination of physiologically active substances, and optionally a pharmaceutically acceptable hydrophilic swelling agent and further pharmaceutically acceptable adjuncts, (b) at least one hydrophilic membrane which surrounds component (a) and which is expansible at the site of use and is permeable to body fluid, and (c) a covering which surrounds component (a) and membrane (b) and which disintegrates without delay under the action of body fluid at the site of use in the stomach), e.g., a gelatin capsule.

As an example, a retard form of this type suitable for the present invention could take the following form. A component (a) is provided in the form of a tablet surrounded by and sealed within component (b) in the form of a hydrophobic membrane or film, the membrane forming a pouch in which the tablet sits. The tablet and membrane assembly are fitted within component (c) provided in the form of a gelatin capsule.

Taken orally, the retard form moves to the stomach where the gelatin capsule disintegrates to release the tablet membrane assembly. Upon contact with stomach fluid, the tablet generates the blowing agent, for example carbon dioxide gas. The gas causes the membrane surrounding the tablet to inflate, forming a gas-filled "bag." This gas-filled "bag" is able to float on the stomach fluids and/or is unable to pass through the pylorus sphincter following inflation, and thus is retained in the stomach. During its dwell time in the stomach, the active ingredients present in the tablet is released slowly and/or in a controlled manner into the surrounding body fluid, preferably by diffusion, through the membrane. Since gastric juice is being transported further into the upper part of the small intestine,

the active ingredient passes continuously and over a prolonged period into the duodenum and jejunum, where it can be absorbed over an extended period. The subject retard form ensures continuous release of the active ingredient in conjunction with uniform absorption. Once the gas generating components are used up, and/or the when the "bag" deflates to a certain size, this allows the remainder of the retard form to pass through the body.

The manufacture of a retard form of the type described above can be complex and includes several challenges. The component (a) or tablet must be sealed within the membranes to form the pouch. Depending on the drug or drugs of choice, the tablet may also contain other excipients which control the release of the drug or drugs from the tablet into the medium of the pouch and subsequently into the gastric fluid of the stomach following diffusion across the pouch into the gastric fluids of the stomach. Once formed, the pouch must be folded to fit within the capsule. While such retard forms can be produced manually, an automated and economical process for producing such forms is desirable to help bring the benefits of the retard form to the public.

Summary of the Invention

The present invention provides a method and apparatus for the automated manufacture of a dosage form that requires folding or wrapping for insertion into a capsule. One such dosage form is a retard dosage form that preferably has at least the following components: 1) a tablet which includes a physiologically active substance or substances and optionally a gas generating substance, 2) a film surrounding the tablet so as to form a pouch (tablet/pouch assembly) that has at least one

flap (the film being preferably hydrophobic), and a capsule surrounding the tablet/pouch assembly and which is capable of disintegrating upon contact with bodily fluids to release the tablet/pouch assembly, the capsule having first and second cap sections. The method includes the steps of providing a continuous strip of multiple pouch assemblies, separating a single tablet pouch assembly from the strip; folding the flap of said tablet/pouch assembly, inserting the folded tablet pouch/assembly into the first cap section to form a tablet/pouch/first cap assembly; and inserting the tablet/pouch/first cap assembly into the second cap section to complete an encapsulation of the tablet/pouch assembly. Other dosage forms are believed possible to which the present invention will apply.

Also provided is a method of making a tablet/pouch assembly of a retard dosage form. One such method includes the steps of providing first and second layers of a hydrophilic film; providing a tablet having a physiologically active substance and a gas generating substance; positioning the tablet between said first and second layers of hydrophilic film; providing a slit in at least one of the two layers; evacuating any gas, e.g., air, between the two layers; and sealing the two layers together to form a sealed tablet/pouch assembly.

Apparatuses for carrying out the above methods is also provided.

Brief Description of the Drawings

The following detailed description will be better understood when read in conjunction with the figures appended hereto. For

the purpose of illustrating the invention, there is shown in the drawings a presently preferred embodiment. It is understood, however, that this invention is not limited to the precise arrangement shown.

Figure 1 is a perspective view of a tablet/pouch assembly for an exemplary retard form;

Figure 1A is a cross sectional view taken along line 1A-1A in Figure 1;

Figure 1B is a perspective view of the encapsulated retard form with the tablet/pouch assembly of Figure 1 inside a capsule;

Figure 2 is a perspective view of a tablet/pouch packaging machine;

Figure 3 is a perspective view of a tablet pouch fold encapsulation machine;

Figure 4 is an illustration of work station 1 of the tablet pouch fold encapsulation machine shown in figure 3;

Figure 4A is a detailed view of work station 1 showing the tablet/pouch assembly on the tooling block;

Figure 5 is an illustration of work stations 2 and 3 of the tablet pouch fold encapsulation machine shown in figure 3;

Figure 6 is an illustration of work station 4 of the tablet pouch fold encapsulation machine;

Figure 6A shows the tablet/pouch assembly within the tooling block at work station 4;

Figure 7 is an illustration of work station 5 of the tablet pouch fold encapsulation machine;

Figure 7A shows the folding arms relative to the tooling block at work station 5 after the folding operation is completed;

Figure 7B is a side view showing the folded tablet/pouch assembly shown in Figure 7;

Figure 8 is an illustration of work station 6 of the tablet pouch fold encapsulation machine where the gel cap bottom is fed into the tooling block;

Figure 8A is a detailed view of the tooling? block at work station 6;

Figure 9 is an illustration of work station 7 of the tablet pouch fold encapsulation machine where the folded tablet/pouch assembly is inserted into the gel cap bottom;

Figure 9A is a detailed view of the tooling? block at work station 7;

Figure 10 is an illustration of work station 8 of the tablet pouch fold encapsulation machine where the folded tablet/pouch assembly is repositioned for further assembly operations;

Figure 10A is a detailed view of the tooling? block at work station 8;

Figure 11 is an illustration of work station 9 of the tablet pouch fold encapsulation machine where the gel cap top is fed into the tooling block;

Figure 11A is a detailed view of the tooling? block at work station 9;

Figure 12 is an illustration of work station 10 of the tablet pouch fold encapsulation machine where the folded tablet/pouch assembly is inserted into the gel cap top;

Figure 12A is a detailed view of the tolling block at work station 10;

Figure 13 is an illustration of work station 11 of the tablet pouch fold encapsulation machine where the completed retard form is inspected and directed to an appropriate container;

Figure 13A is a detailed view of the tooling? block at work station 11;

Figure 14 shows the tablet/pouch packaging machine and the tablet pouch fold encapsulation machine, the tablet pouch fold encapsulation machine shown within an enclosure; and

Figure 15 shows an example of a vision control system.

Detailed Description of the Invention

The present invention provides a novel method for making a retard dosage form. The method of the present invention permits automation of the manufacturing process and thus allows the economical manufacture of such dosage forms. An apparatus for carrying out the method of the present invention is also provided.

An exemplary retard form (designated item #10 in the accompanying drawings) to be manufactured in accordance with the present invention is illustrated with reference to Figures 1, 1A and 1B. Figure 1B shows the completed encapsulated retard dosage form 10 which is now described in further detail.

With particular reference to Figs 1 and 1A, the retard form has a tablet 12, component (a) above, which contains the desired physiologically active ingredients, excipients, and blowing agents. The tablet 12 is preferably formed in a flattened capsule shape, having dimensions of about 3mm height and maximum length and width of about 16mm long by 6mm wide. Nominal tablet weight is 640-750mg, and tablet hardness approximately 50 Newtons. Other shapes and configurations may be suitable.

Surrounding the tablet 12 is a film or membrane 14 configured to form a pouch 16, which is inflatable upon the generation of gas from the tablet 12 within to form a gas-filled "bag." The membrane is preferably provided in two layers, a bottom layer 14a and top layer 14b, with the tablet 12 sandwiched in between. The two membrane layers 14a, 14b are heat sealed together to form a sealed pouch 16, and form side flaps 15a, 15b extending from both sides of the tablet 12 as shown (there may

also be front and back flaps 17a, 17b). The membrane film preferred is a polyvinylaclcohol (PVA) having a thickness of approximately 150 μm (± 10 μm), and which is typically formed of two membrane layers sealed together. The pouch 16 is preferably between about 20mm x 20mm and 25mm x 25mm inside dimensions. The seal width is about 2 to 3mm in addition to the inside dimensions indicated all around the pouch. The combination tablet and pouch will be referred to herein as the tablet/pouch assembly 18.

Surrounding the tablet/pouch assembly 18 is a capsule 20 having first and second capsule sections 20a, 20b, respectively, component (c) above, which disintegrates quickly when exposed to the stomach fluids to release the tablet/pouch assembly 18. See Figure 1B. The capsule is preferably gelatin, having a size range preferably of 0EL and 00EL. The tablet/pouch assembly 18 is fitted inside the capsule in a folded, compact form. Once the capsule disintegrates, the tablet/pouch assembly 18 can open to its unfolded form and, upon contact with the bodily fluids, inflate to form the "bag" as described previously.

One method of making the retard form 10 of the present invention begins with the manufacture of the tablet/pouch assembly 18. Shown in Figure 2 is a tablet/pouch packaging machine 24 for producing a strip of attached tablet/pouch assemblies 18, each of the assemblies being of the type illustrated in Figures 1 and 1A. A tablet hopper 26 receives and holds the tablets 12 which are produced through methods known in the art. A first spool 28 of film 14 is provided for forming the first or lower membrane layer 14a, and a second spool 30 of film 14 is provided for forming the second or upper membrane layer

14b. The spools are automatically maintained at the proper tension.

A tablet 12 is controllably released from the hopper 24 onto the lower membrane layer 14a in the desired orientation. The upper membrane layer 14b is then laid on top of the tablet 12. (With films that have a backing, the backing is rewound for removal and disposal). The machine 24 automatically punches a hole in at least one of the films 14a, 14b through which air can be evacuated during a subsequent sealing process. Alternatives are possible. With the tablet sandwiched between the two films 14a, 14b, the films are pressed together and the air between the two layers evacuated through the punched hole to a desired vacuum level. The two films are then sealed together with a heating element pressed into contact with the film to produce a seal around the tablet 12, preferably air tight, of about 2 to 3mm in width (the air evacuation hole being on the outside of the seal), thereby forming the sealed tablet/pouch assembly 18. The sealing temperature is preferably between 200 - 210 °C with a dwell time of about two seconds. The machine 24 can produce multiple tablet/pouch assemblies 18 during each cycle, the completed tablet/pouch assemblies forming a continuous strip 32 of tablet/pouch assemblies 18 which can be rolled up into a spool 34, or fed directly to a tablet pouch fold encapsulation machine for further processing as described below. The machine 24 can be controlled by a programmable controller as known in the art. Other evacuation and sealing methods are contemplated. For example, three of the four sides of the films/tablet assembly could be heat sealed first, then the air evacuated from the pressed films/tablet assembly on the unsealed side, followed by sealing the last side. Moreover, the tablet can be inserted into

the pouch after the three sides are sealed, the fourth side then being sealed after the tablet is inserted and the air evacuated by vacuum.

With reference to Figure 3, the tablet pouch fold encapsulation machine 38 is now described. The encapsulation machine 38 receives the tablet/pouch assembly 18 and, through the automated steps described below, produces a completed encapsulated tablet/pouch assembly (retard dosage form) 10. As seen in Figure 3 the machine 38 has a rotatable table 42 mounted on a frame 43 and has multiple tooling blocks 44 (see Fig. 4A) mounted thereon along the outer edge of the table, each tooling block 44 capable of receiving and carrying one tablet/pouch assembly 18 for processing. The table 42 rotates to move the tablet/pouch assembly 18 to the different work stations where the various manufacturing steps are performed. An upper support table 58 supports equipment as described below. The rotation of the table 42 is controlled by a controller or other suitable automated means controlling a motor as is known in the art to move the tablet/pouch assemblies 18 to the multiple work stations where the various steps are performed to produce the final encapsulated product 10.

With reference to Figures 3 and 4, a continuous strip 32 of tablet/pouch assemblies 18 is delivered to the machine 38 at a work station one (WS1) either directly from the tablet/pouch packaging machine 24 or from the spool 34 as shown in Figure 3. The strip 32 moves through a slotted strip puller 48 where a single tablet/pouch assembly 18, resting on a slotted support shelf 50, is sheared off from the incoming strip 32 by a rotary cutter 52 having blades 54.

With further reference to Fig 4A, a pick and place unit 56, such as that which uses a suction to pick and hold an item and a vision system to control the placement, picks the sheared tablet/pouch assembly 18 from the shelf 50 and places it on the tolling block 44 directly above a tooling pocket 60. As seen in Fig. 4A, the tooling block 44 has a cylindrical passageway 62 extending longitudinally through the block 44 and which has openings 64a, 64b on both sides of the block 44. The tooling pocket 60 extends downward from the top face 66 of the block 44 to the cylindrical passageway 62. Bolts 68 connect the tooling block 44 to the table 42. Slidable on the top face 66 of the block 44 are left and right folding arms 70a, 70b. The folding arms 70a, 70b are slidable in the slightly recessed or grooved area 72 toward the tooling pocket 60 for folding the tablet/pouch assembly 18 as described below. The recessed area 72 is at about the same elevation as the top of the cylindrical passageway 62.

With reference to Fig. 5, after placement of the tablet/pouch assembly 18 onto the tooling block 44 at station one (WS1), the table 42 is rotated to bring the tablet/pouch assembly 18 to work station two WS2, where a vision camera 76 inspects the pouch 16 of the assembly 18 for a good seal and the tablet 12 for breakage. Visions systems are known in the art, an example of one being shown in Figure 15. A normal lens with a red LED backlight produced images that were better for finding broken tablets and bubbles. A telecentric lens with telecentric backlight produced images that were better for finding the seal edge. Should the tablet/pouch assembly 18 be defective, it is removed at work station three WS3 where the table 42 brings the tablet/pouch assembly 18 under a vacuum transducer 80. If not defective, the

tablet/pouch assembly 18 continues with the rotation of the table 42 to work station four WS4.

With reference to Figs. 6 and 6A, at work station four (WS4) the tablet/pouch assembly 18 is inserted into the tooling block 44 to begin the folding of the pouch. Supported above the tablet/pouch assembly 18 on the upper support 58 is an arm 84 having a ram 86. The ram 86 is extendable from the retracted position shown in Figure 6 to an extended position whereby it pushes the tablet/pouch assembly 18 down into the tooling pocket 60 and into the cylindrical passageway 62. The ram 86 has a head 88 shaped to correspond with the shape of the top of the tablet/pouch assembly 18 so as not to cause any damage. Different rams 86 with different head 88 shapes may be used to for corresponding with different shapes of the assembly 12.

With reference to Figure 6A, it is seen that as the tablet/pouch assembly 18 is pushed downward into the tooling pocket 60, the side flaps 15a, 15b of the pouch 16 are folded upward about the tablet 16, leaving the side flaps 15a, 15b extending upwards and out of the tooling pocket 60. Once the ram 86 is retracted, the table 42 moves the tablet/pouch assembly 18 (in the tool block) to work station five WS5 for further folding.

With reference to Figures 7, 7A and 7B, work station five (WS5) is where the final folding operation takes place. An arm 92 at work station five has pins 94 for engaging the openings 96 in the folding arms 70a, 70b. For the final folding operation, the arm 92 is lowered so that the pins 94 can engage the openings in the folding arms. Any type of suitable actuator or motor

device 93 may be used for moving the pins to move the arms. First, the right folding arm 70a is moved towards the left to fold the right side flap 15b of the pouch 16 approximately 90 degrees towards the left (see also Fig. 6A). Then the left folding arm 70b is moved to the right to fold the left side flap of the pouch 16 approximately 90 degrees to the right. The right folding arm 70a then retracts to clear the opposite end of the pouch, and the left folding arm 70b moves to the right to fully cover and trap the folded pouch within the cylindrical passageway 62 as shown in Fig. 7B. The folded tablet/pouch assembly 18 is now ready for encapsulation.

At work station six (WS6), with reference to Figures 8 and 8A, the opening 64b to the cylindrical passageway 62 on the back side of the block 44 aligns with a feed tube 100 which delivers the gel cap bottom 20a to the tooling block 44. A bowl feeder 102 (Fig. 3) supplies a single gel cap 20a properly oriented through means as known in the art through the feed tube 100 to the tooling block 44 as shown.

The tooling block 44 with the gel cap 20a next proceeds to work station seven (WS7) where the folded tablet pouch assembly 18 is inserted into the gel cap bottom 20a. With reference to Figures 9 and 9A, a horizontal ram 106 extends from a ram actuator 108 through the passageway 62 to push the tablet/pouch assembly into the gel cap bottom 20a. A holding means, such as a blocking plate moved to the back opening 64a prevents the cap 20a from moving. The horizontal ram 106 is then retracted to clear the tooling block 44. The ram actuator 108 is supported on the frame 43 of machine 24.

At work station eight (WS8), with reference to Figures 10 and 10A, the folded tablet/pouch assembly 18 in the bottom cap 20a is repositioned within the passageway 62 for further processing. Here a horizontal ram 111 supported on the frame 43 extends through the passageway 62 to transfer the tablet/pouch/cap assembly out the back side of the tooling block 44 and into a pick and place gripper. The pick and place gripper then transfers the tablet/pouch/cap assembly to the front end of the tooling pocket 60 in the passageway 62. As an alternative, which is not shown, a ram could simply push the tablet towards the front of the tooling pocket60 in the passageway 62.

At work station nine (WS9), with reference to Figures 11 and 11a, the front opening 64a of the passageway 62 aligns with a second feed tube 112 through which the gel cap top 20b is delivered to the tooling block 44. A bowl feeder 114 supplies a single cap top through the feed tube 112 as shown (see Fig. 3).

The tooling block 44 next proceeds to work station ten (WS10) where the folded tablet/pouch/cap top assembly is inserted into the gel cap top 20b. With reference to Figures 12 and 12A, a rear horizontal ram 120 extends from a ram actuator 122 through the passageway 62 to push the tablet/pouch/cap bottom assembly into the gel cap top 20b, which is held in place by a front horizontal ram 124 which extends from the front ram actuator 126. The front edges of the two rams are shaped to correspond with the shape of the gel caps to prevent damage to the gel caps. After the top and bottom gel caps 20a, 20b are attached, both rams 120, 124 are retracted to clear the tooling block 44. Next the two folding arms 70a, 70b are retracted by an actuated arm 130 having pins 131 for interfacing with the folding arms.

With reference to Figures 13 and 13A, the final process step at work station eleven (WS11) is described. Here, the final retard form 10 (the combined gel cap/tablet/pouch assembly) is inspected and directed to the appropriate container. A horizontal push rod 132 is extended into the passageway 62 to expel the retard form 10 from the tooling block 44 onto a support shelf 134 where it can be inspected by a camera 136. If the assembly 10 is acceptable, the push rod 132 extends further to push the assembly 10 into the acceptable bin, otherwise, if rejected, the assembly 10 is ejected into a reject container. This can be accomplished with a diverter arm (not shown) controlled by a controller which diverts the assembly between two chutes or troughs that directs the assembly to the acceptable bin or the reject container.

The table 42 then rotates to bring the tooling block 44 back to work station one (WS1) where a new tablet/pouch assembly 18 is received for encapsulation. It is seen that the table 42 has multiple tooling blocks 44 for processing tablet pouch assemblies in a continuous automated process.

With reference to Figure 14, the machines can be encased within a housing 140 having interlocked safety doors 142 and covers to prevent inadvertent injury to personnel or product contamination. Any suitable control system for controlling the various process steps may be used. For example, machine controls and parameter adjustments can be executed via an operating console 144 as shown in Figure 14.

The present invention as described above provides an economical means of producing an advantageous retard dosage form.

While particular embodiments of the invention are described herein, it is not intended to limit the invention to such disclosure and changes and modifications may be incorporated and embodied within the scope of the invention.

What is claimed is:

1. An automated process for making a retard dosage form, said process comprising the following machine steps:

(A) providing a continuous strip of multiple pouch assemblies, each of said tablet pouch assemblies comprising a physiologically active substance sealed within a membrane;

(B) separating a single tablet pouch assembly from said strip;

(C) folding said membrane to form a folded tablet pouch assembly;

(D) inserting said folded tablet pouch assembly into a first cap section to form a tablet/pouch/first cap assembly; and

(E) inserting said tablet pouch assembly into a second cap section.

2. The automated process of claim 1 further comprising the following steps carried out prior to step (A):

(F) positioning a tablet between two layers of a film; and

(G) sealing together said two layers of step (F) so as to form a pouch, said tablet being sealed within said pouch.

3. An automated process for making a retard dosage form having at least the following components: 1) a tablet which includes a physiologically active substance, 2) a film surrounding the tablet so as to form a pouch (tablet/pouch assembly) that has at least one flap, and a capsule surrounding the tablet/pouch assembly and which is capable of disintegrating upon contact with bodily fluids to release the tablet/pouch assembly, said capsule having first and second cap sections; said process comprising the following automated machine steps:

(A) providing a continuous strip of multiple said pouch assemblies, each of said tablet pouch assemblies;

(B) separating a single tablet pouch assembly from said strip;

(C) folding said flap of said tablet/pouch assembly;

(D) inserting said folded tablet pouch/assembly into the first cap section to form a tablet/pouch/first cap assembly; and

(E) inserting said tablet/pouch/first cap assembly into the second cap section to complete an encapsulation of the tablet/pouch assembly.

4. The automated process for making a retard dosage of claim 3 wherein step (B) comprises the step of cutting said single tablet/pouch assembly from said strip with a blade or a laser.

5. The automated process for making a retard dosage of claim 3 wherein step (C) comprises the step of using an arm to push the flap over the tablet pouch/assembly.

6. The automated process for making a retard dosage of claim 3 wherein steps (D) and (E) comprise the steps of pushing said folded tablet/pouch assembly into said first cap section, and then pushing said folded tablet/pouch assembly with said first cap section into said second cap section.

7. The automated process for making a retard dosage of claim 3 further comprising the step of inspecting said tablet/pouch assembly for damage after step (B) using an optical inspection equipment.

8. A method of making a tablet/pouch assembly of a retard dosage form; said method comprising the steps of:

(A) providing first and second layers of a film;

(B) providing a tablet having a physiologically active substance;

(C) positioning said tablet between said first and second layers of film;

(D) providing a slit in at least one of said two layers;

(E) evacuating any gas, e.g., air, between said two layers; and

(F) sealing said two layers together to form a sealed tablet/pouch assembly.

9. The step of claim 8 wherein step (E) comprises the use of a vacuum and step (f) comprises heat healing said two layers.

10. An apparatus for the automated manufacture of a retard dosage form having at least the following components: 1) a tablet which includes a physiologically active substance, 2) a film surrounding the tablet so as to form a pouch (tablet/pouch assembly) that has at least one flap, and a capsule surrounding the tablet/pouch assembly and which is capable of disintegrating upon contact with bodily fluids to release the tablet/pouch assembly, said capsule having first and second cap sections; said apparatus comprising the following:

a tooling block movable to multiple work stations where various manufacturing processes are carried out; said tooling block having a passageway extending longitudinally there through and which is configured for receiving said tablet/pouch assembly which is slidable therein, a tooling pocket extending from a top surface of said tooling block to said passageway and which is

configured for receiving said tablet/pouch assembly;

a ram disposed to push the tablet/pouch assembly through said tooling pocket to said passageway;

at least one folding arm for folding the flap of said tablet/pouch assembly extending from said passageway, said folding arm being moveable relative to said tooling block;

a first horizontal ram for pushing said tablet/pouch assembly through said passageway into said first cap section; and

a second horizontal ram for pushing said tablet/pouch assembly through said passageway into said second cap section.

11. The automated process of claim 2 wherein said film in step (F) is a hydrophobic film.

12. The process of claim 3 wherein said tablet further includes a gas generating substance.

13. The method of claim 8 wherein said first and second layers of step A are a hydrophobic film.

14. The method of claim 13 wherein said tablet of step (B) further has a gas generating substance.

15. A method of making a tablet/pouch assembly of a dosage form; said method comprising the steps of:

(A) providing first and second layers of a film;

(B) providing a tablet having a physiologically active substance;

(C) positioning said tablet between said first and second layers of film;

(D) evacuating any gas, e.g., air, between said two layers;

and

(E) sealing said two layers together to form a sealed tablet/pouch assembly.

Abstract

An automated process and apparatus for making a dosage form. The method includes the following steps: providing a continuous strip of multiple pouch assemblies, each of the tablet pouch assemblies include a physiologically active substance sealed within a membrane; separating a single tablet pouch assembly from the strip; folding the membrane to form a folded tablet pouch assembly; inserting the folded tablet pouch assembly into a first cap section to form a tablet/pouch/first cap assembly; and inserting the tablet pouch assembly into a second cap section. A method for making the tablet/pouch assembly is provided. Also provided are apparatuses for carrying out the above methods.

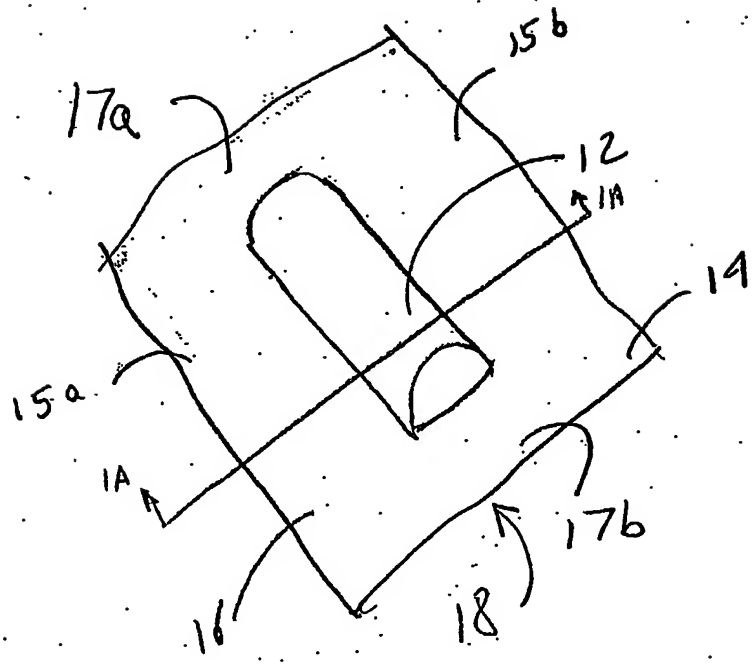

FIG 1

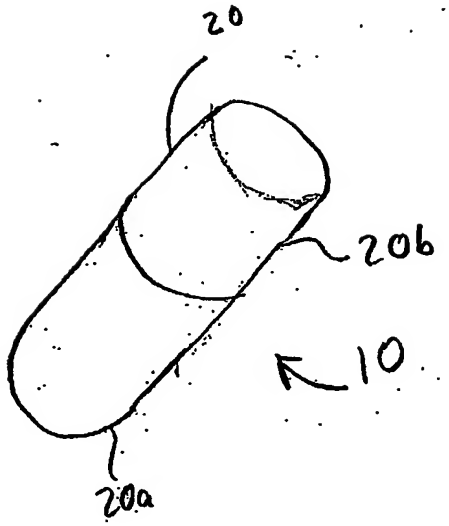

FIG 1B

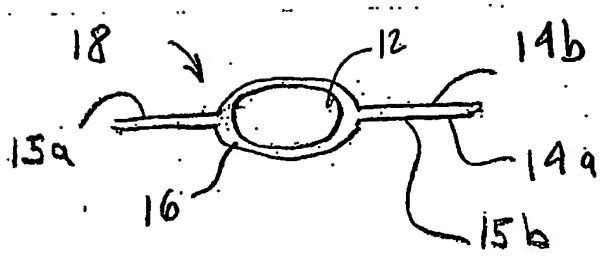

FIG 1A

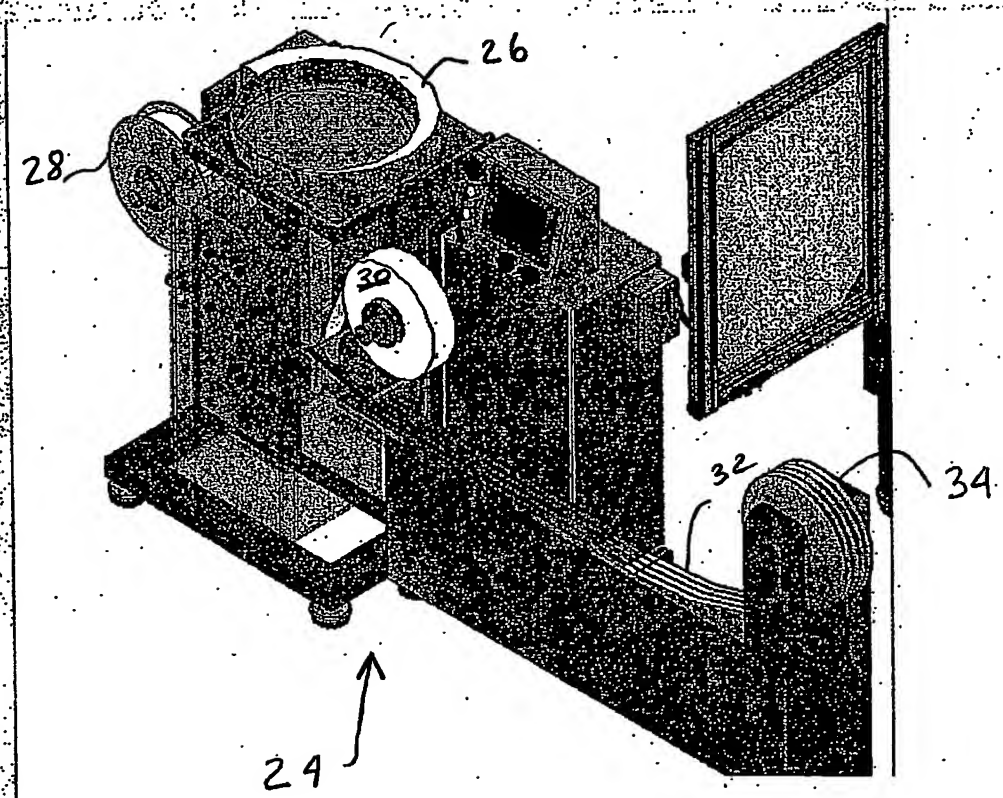

FIG 2

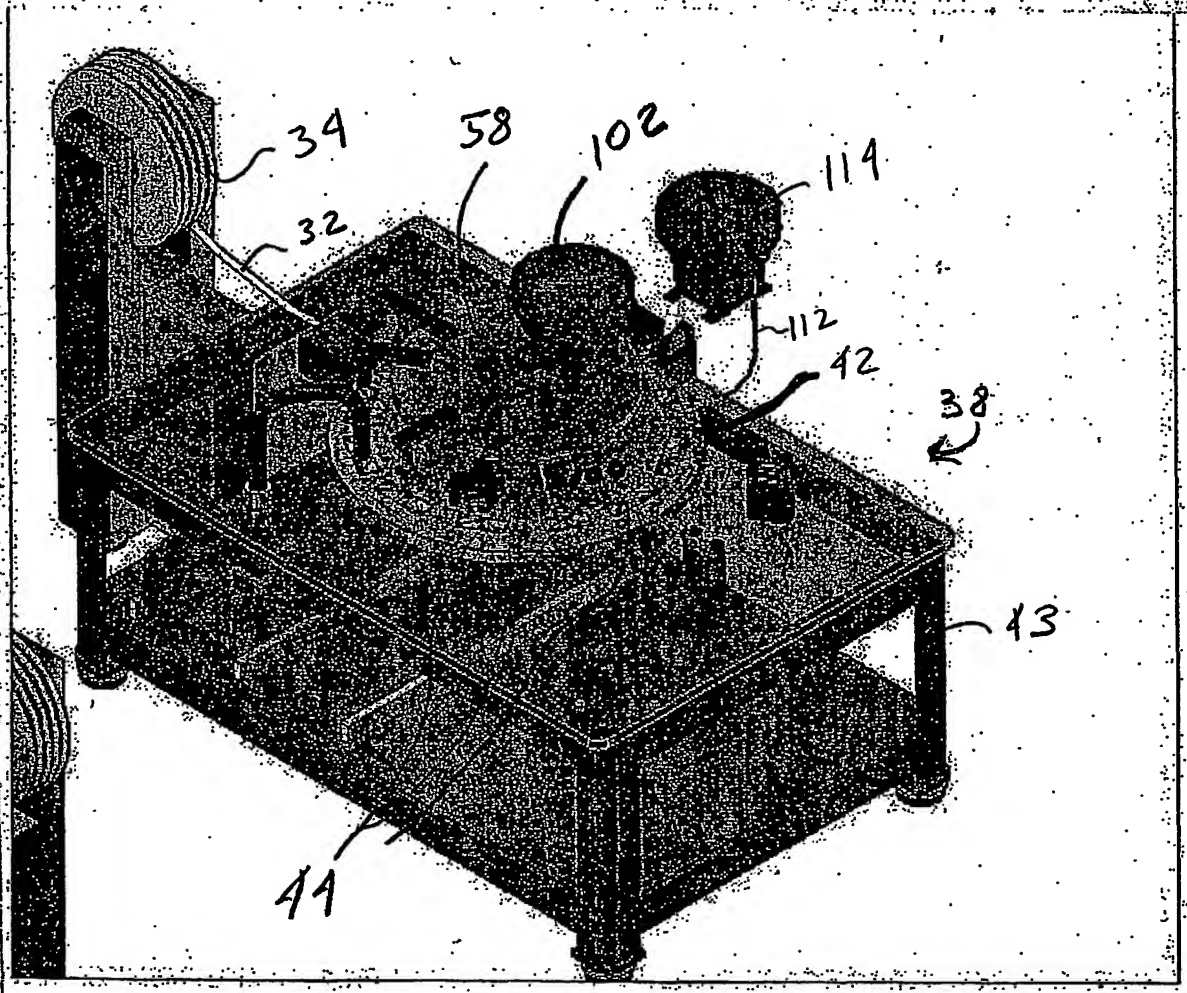

FIG 3

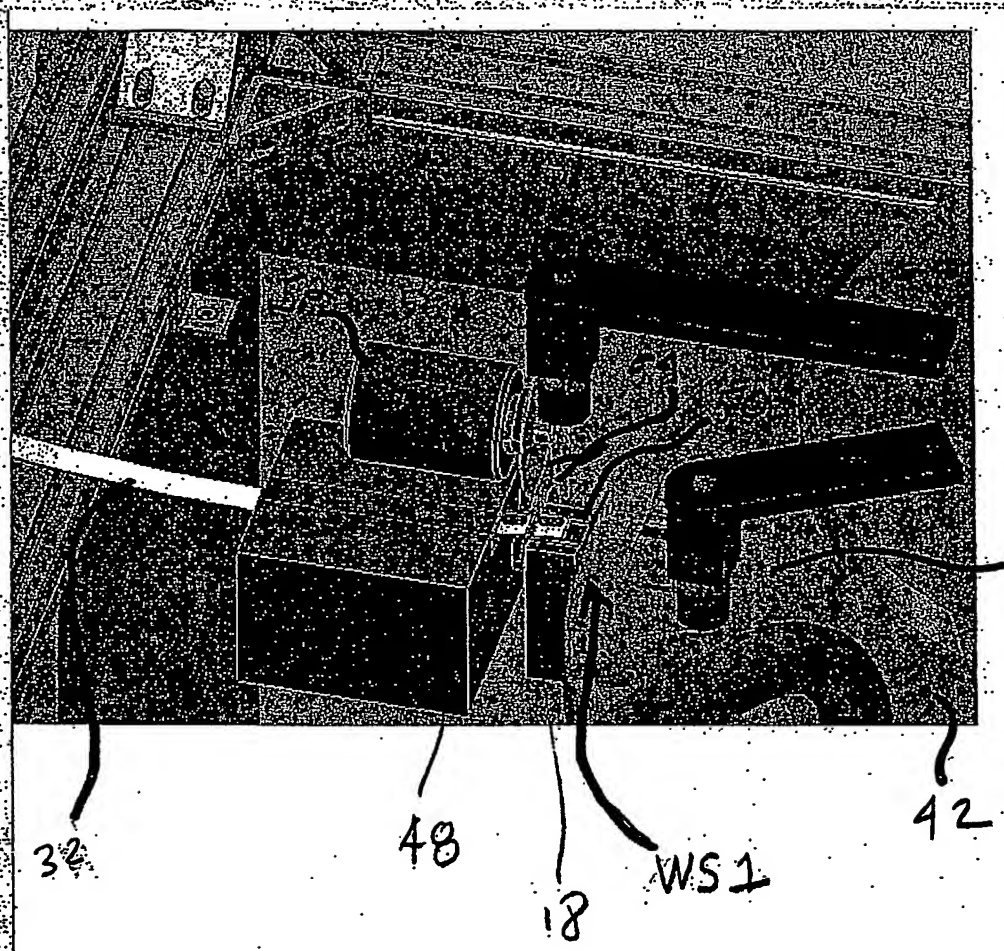

FIG 4

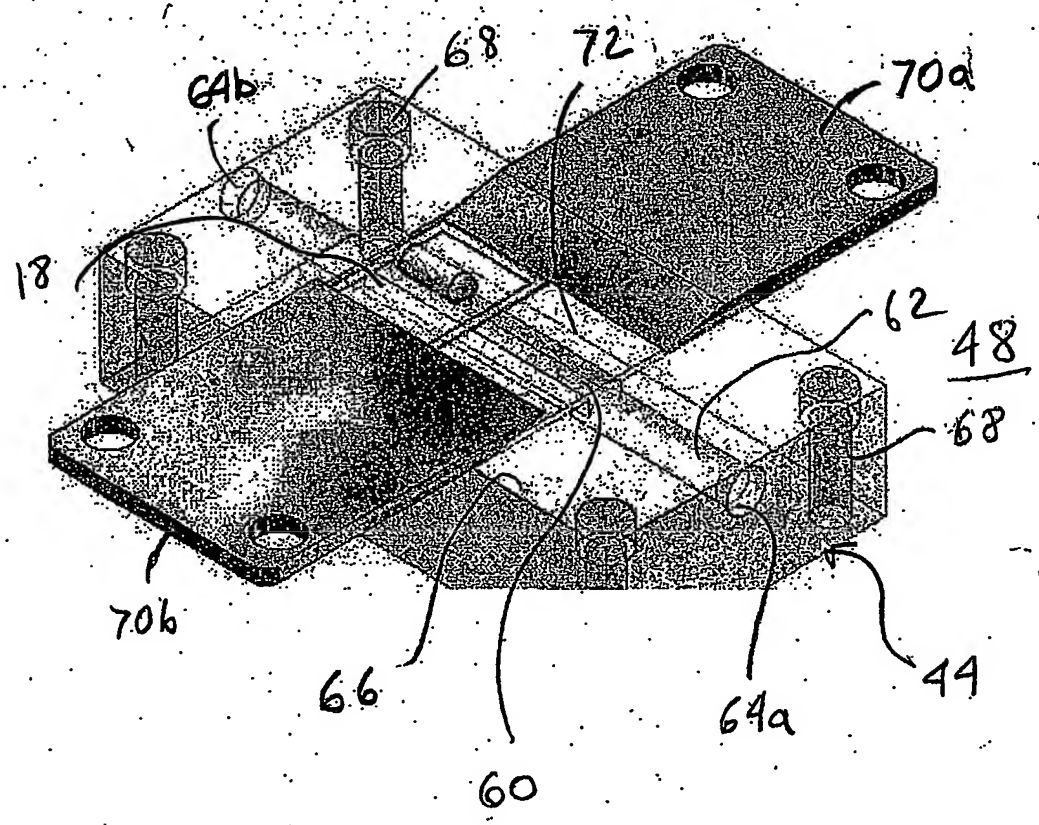

FIG. 4A

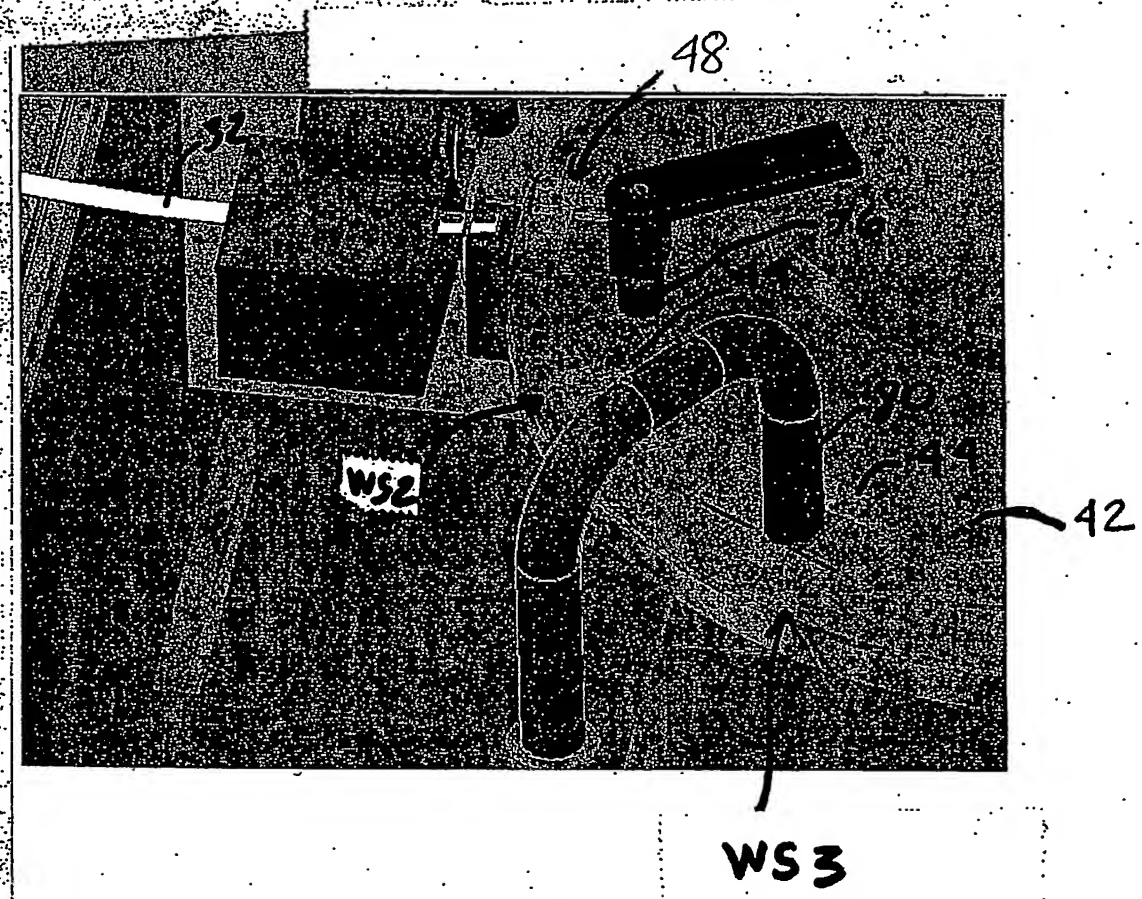

FIG 5

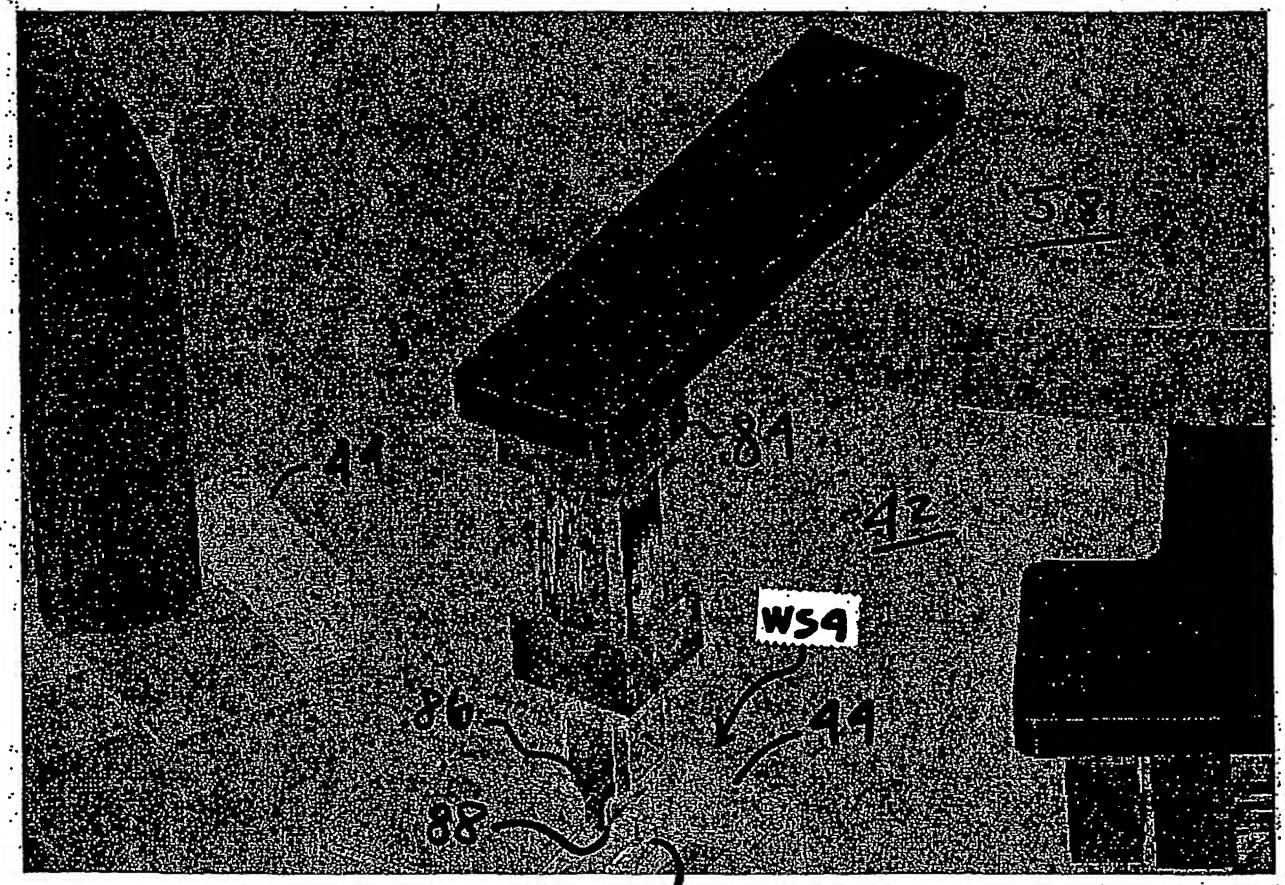

FIG 6

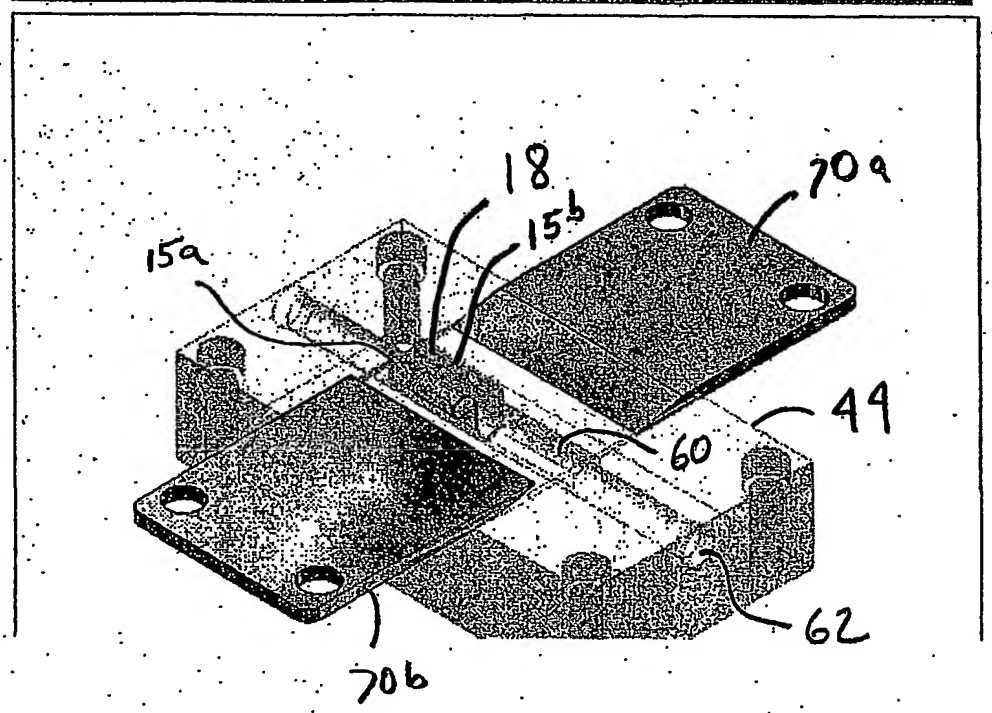

FIG 6A

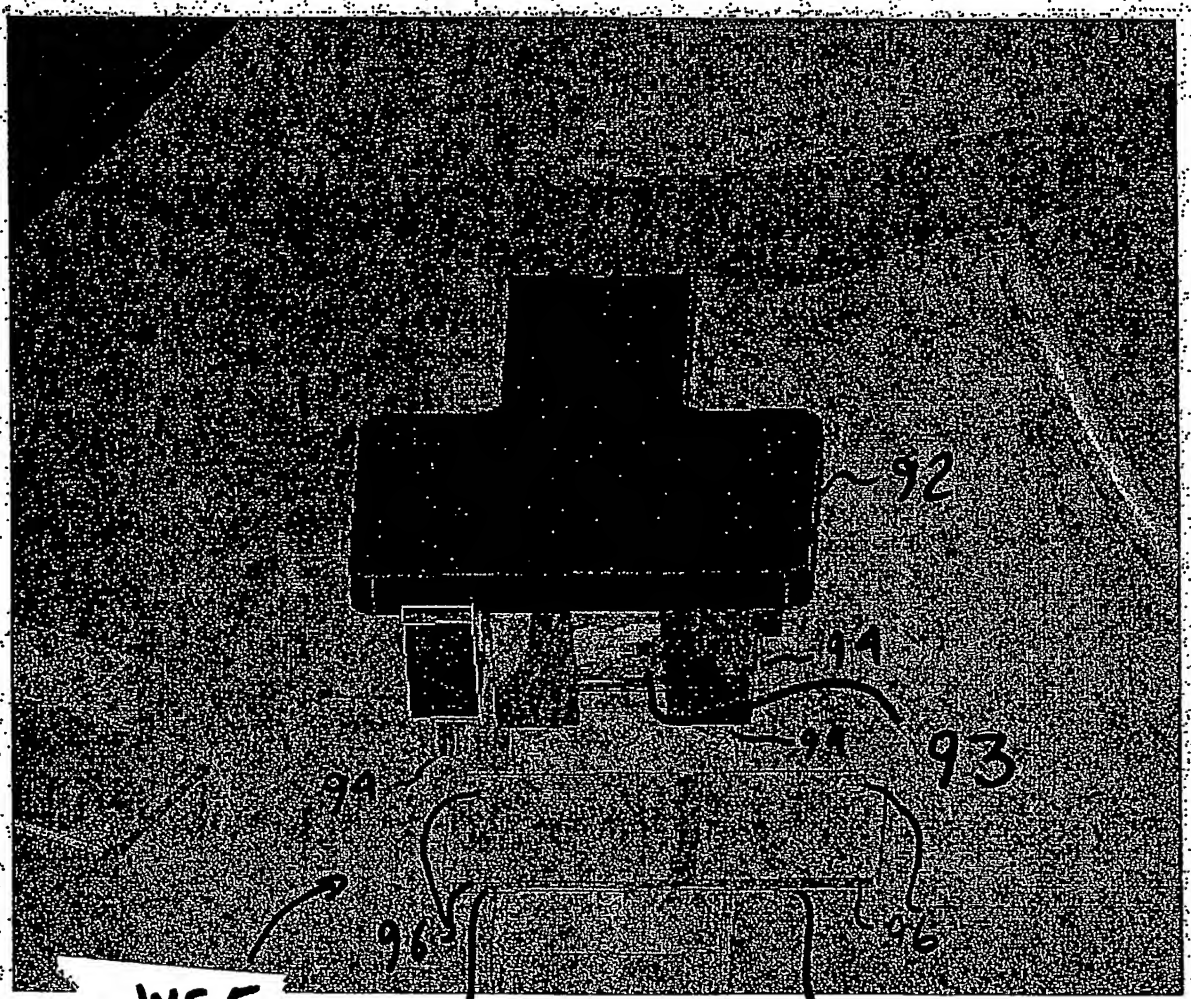

FIG 7

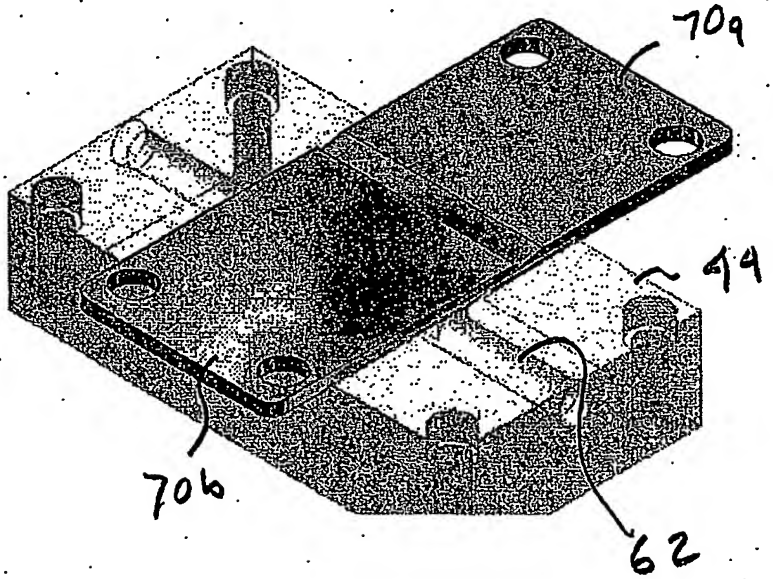

FIG 7A

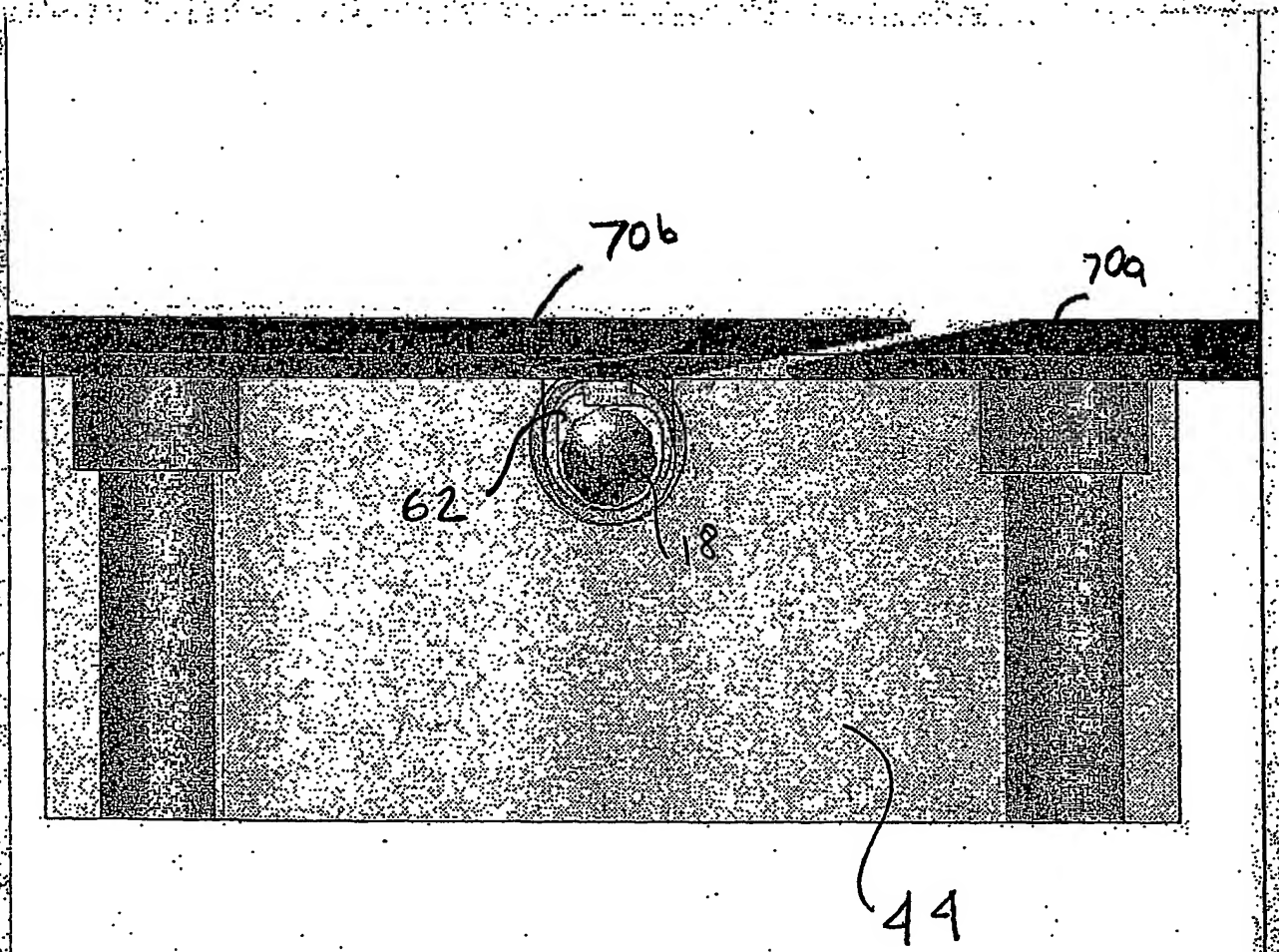

FIG. 7B

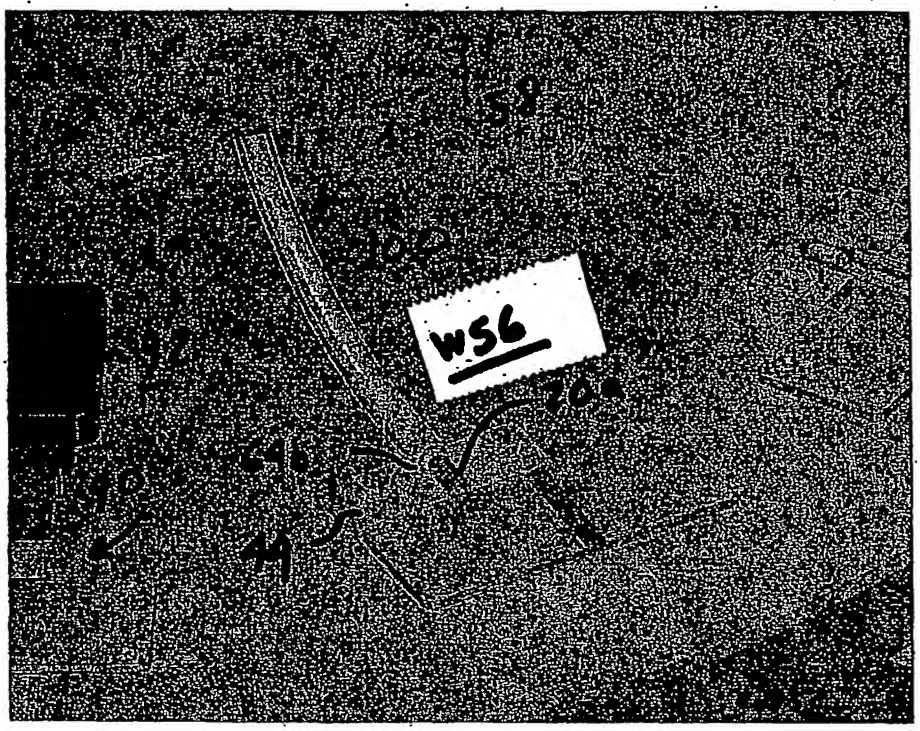

FIG 8

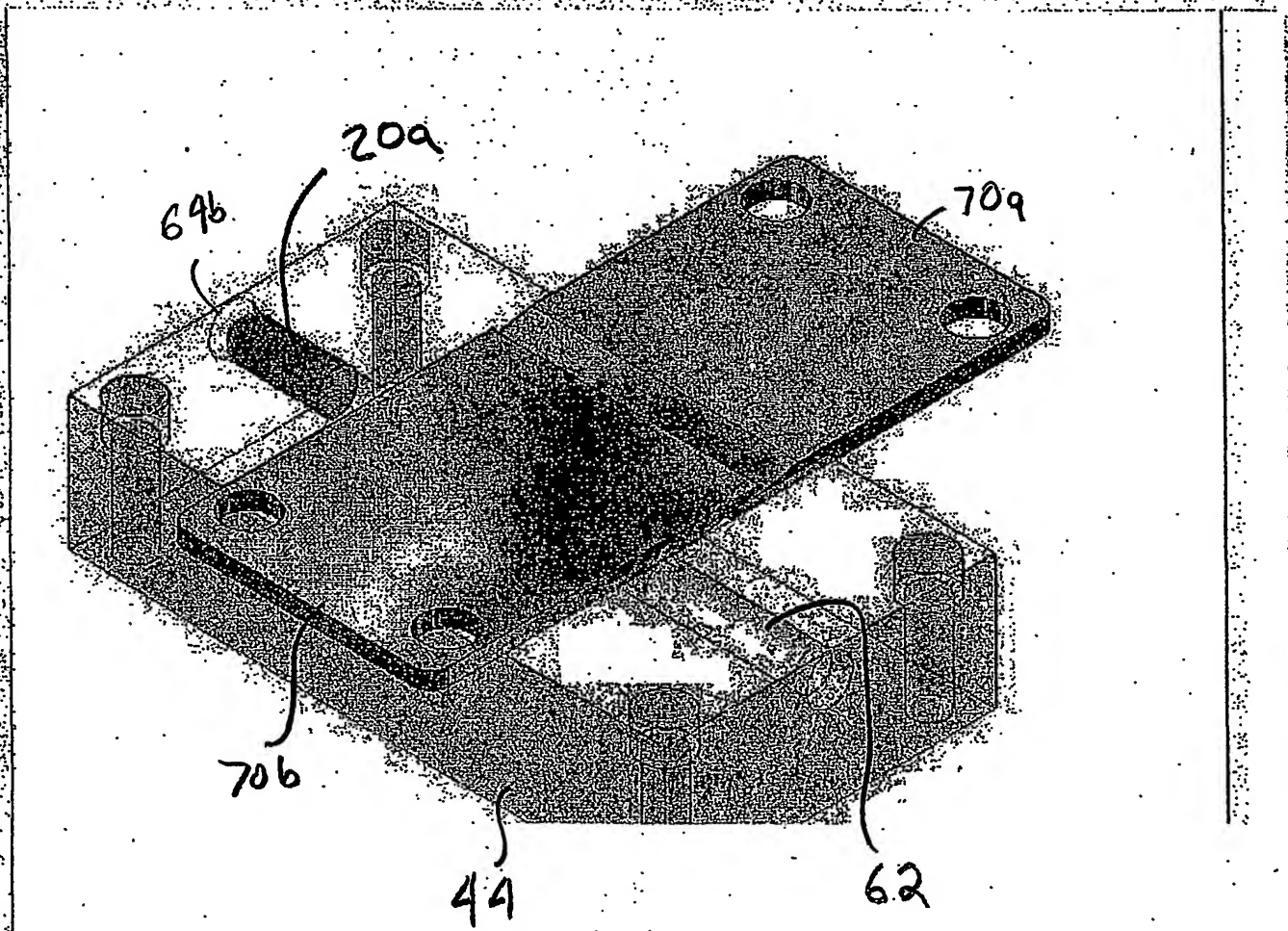

FIG 8A

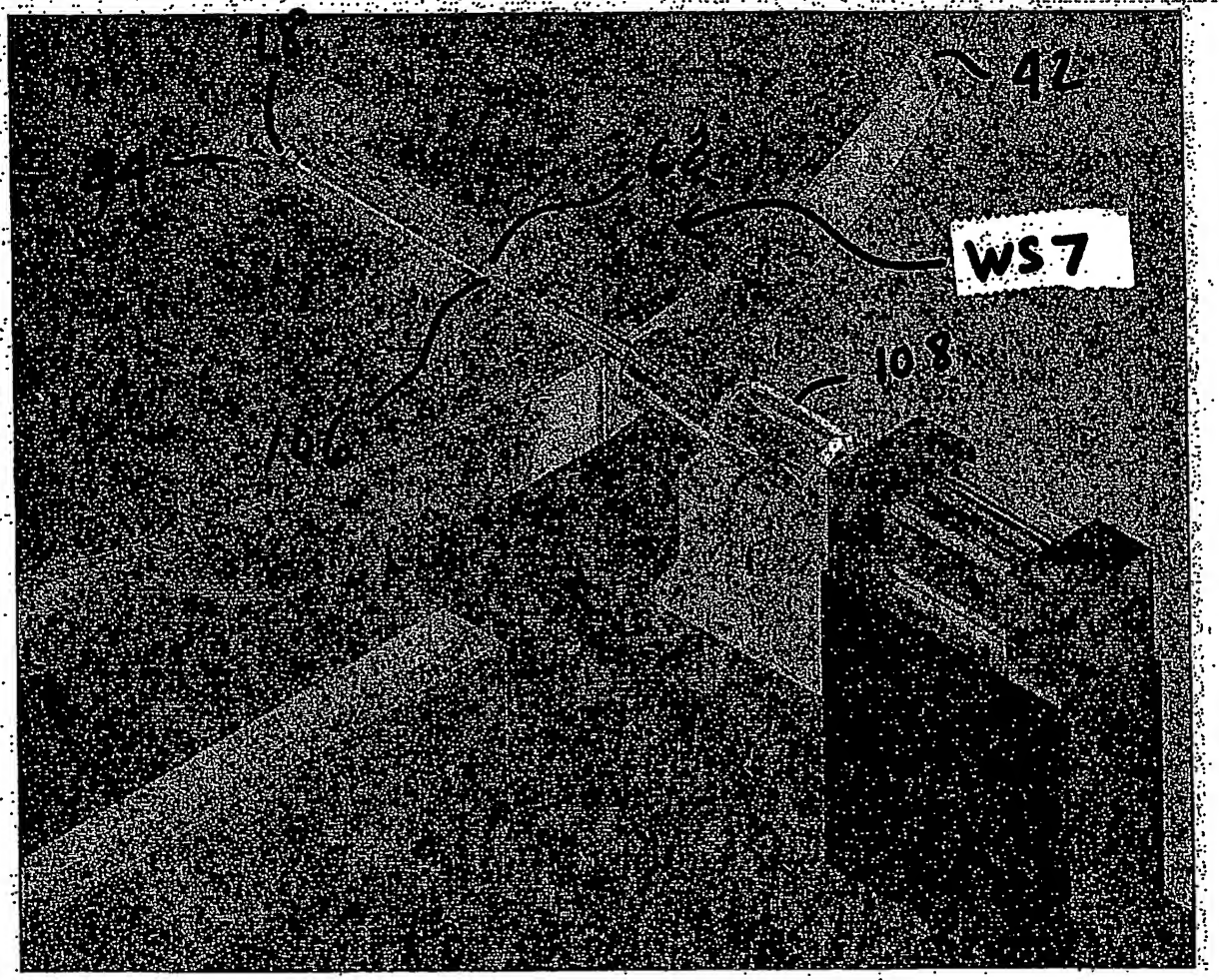

FIG 9

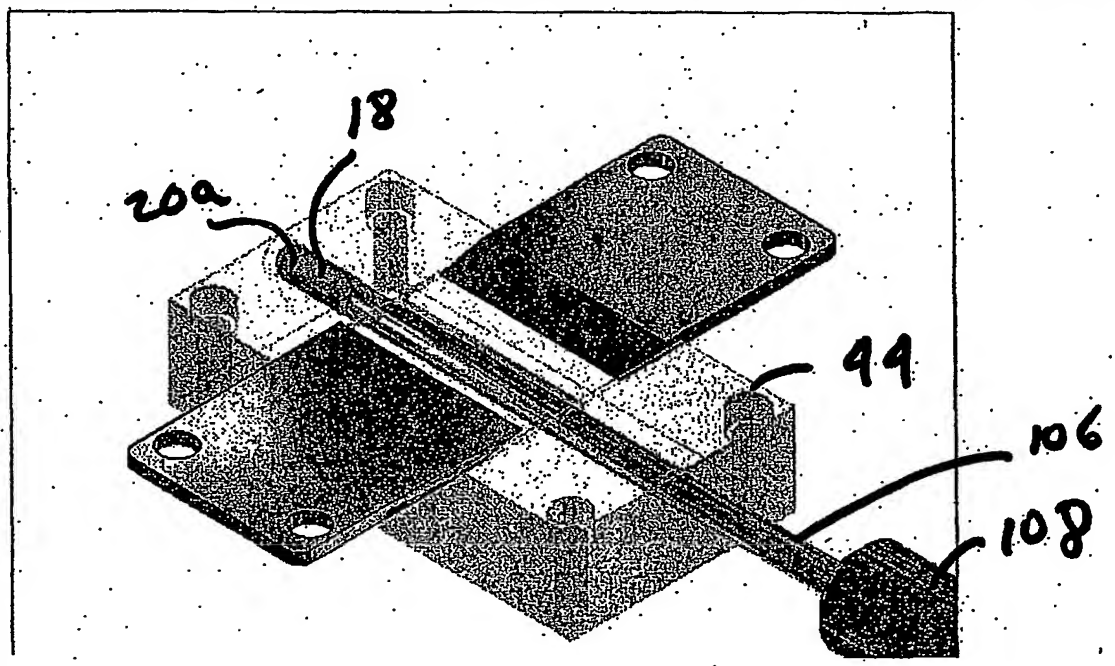

FIG 9A

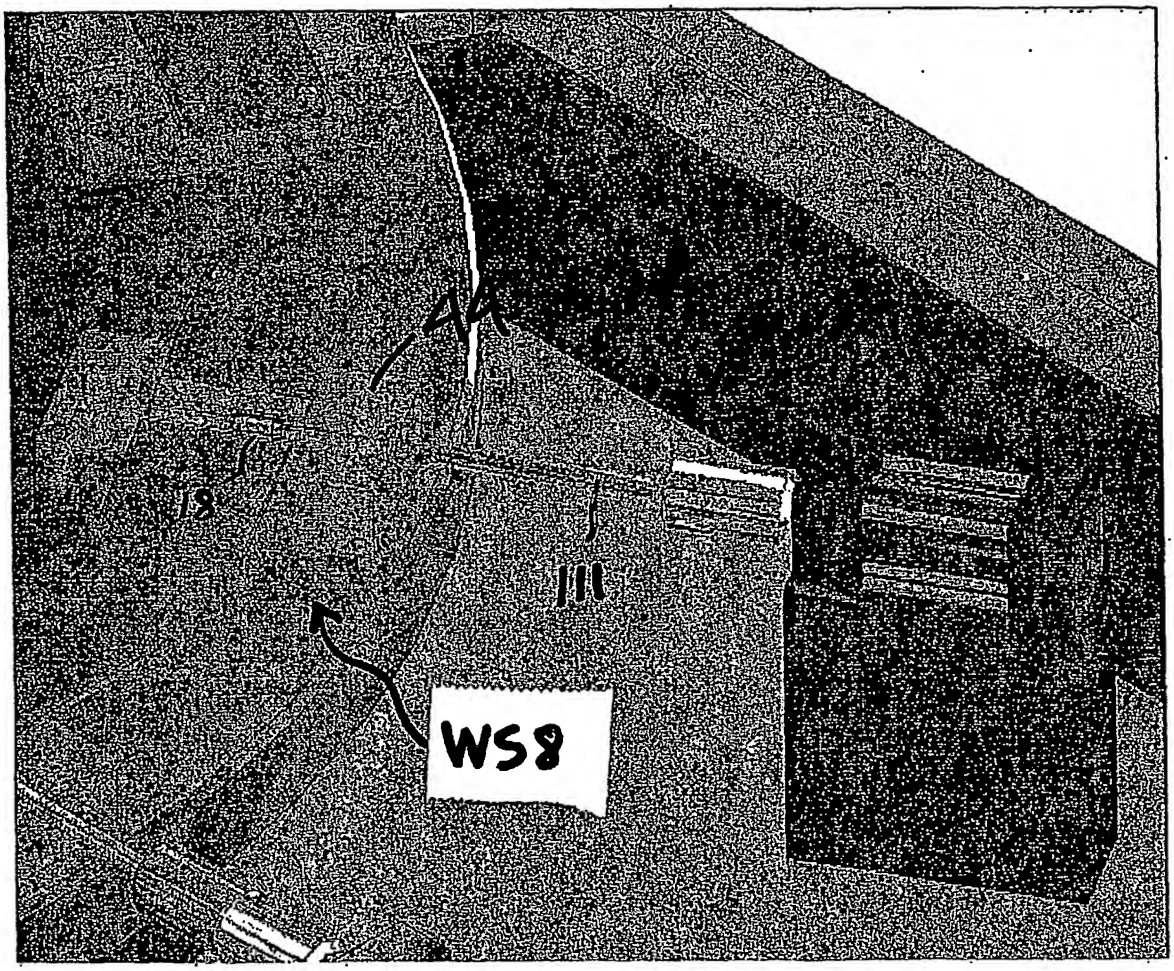

FIG 10

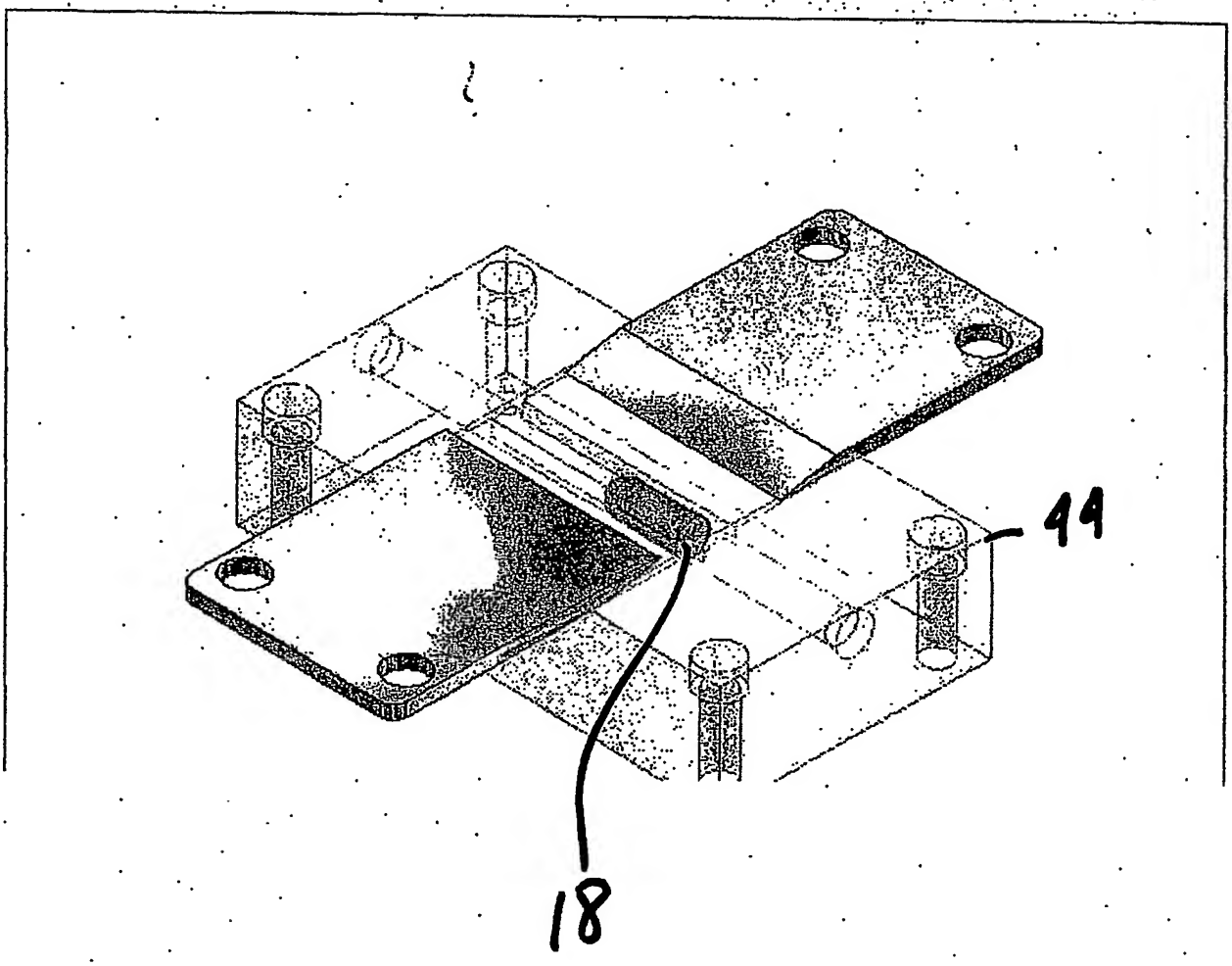

FIG 10A

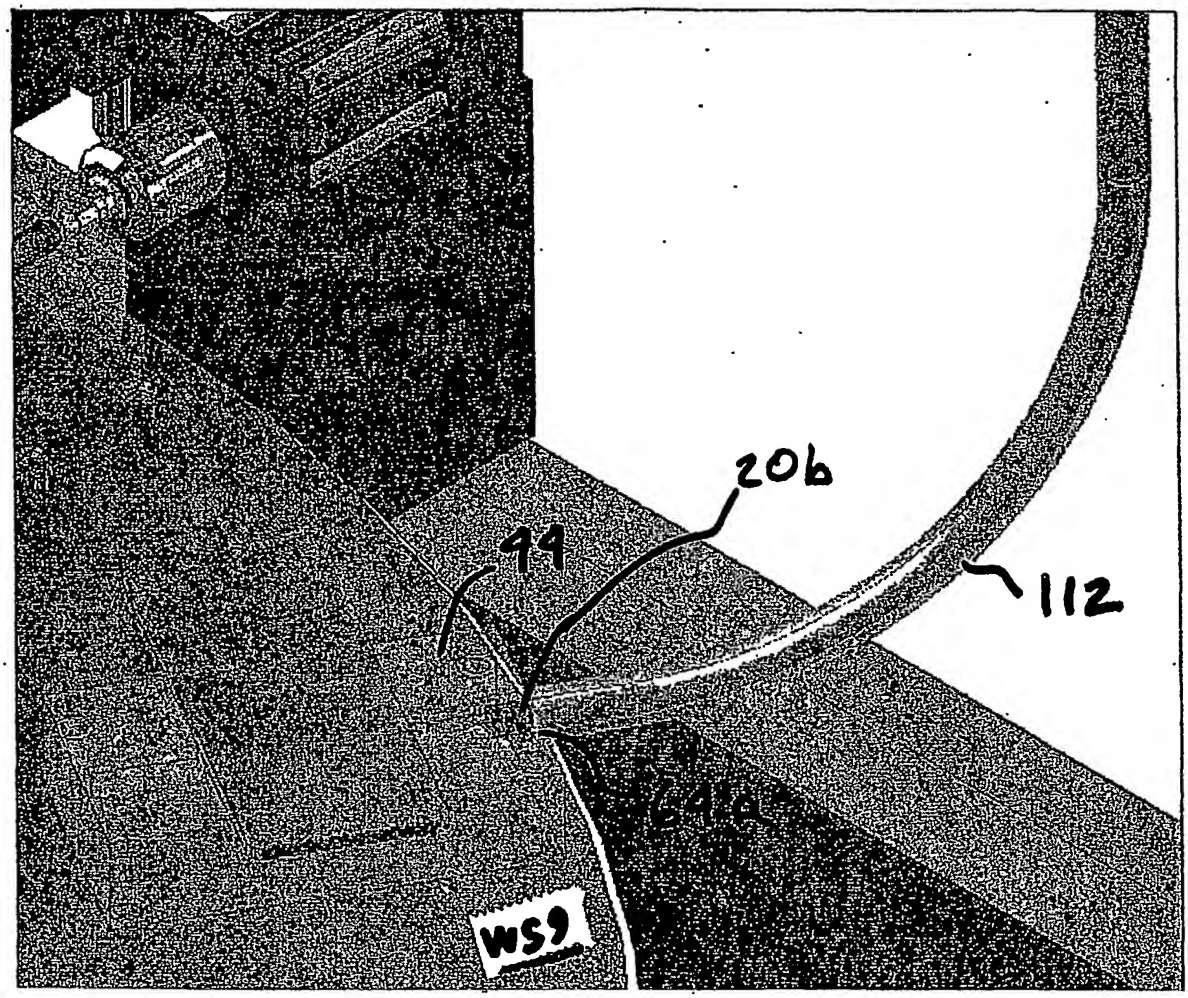

FIG 11

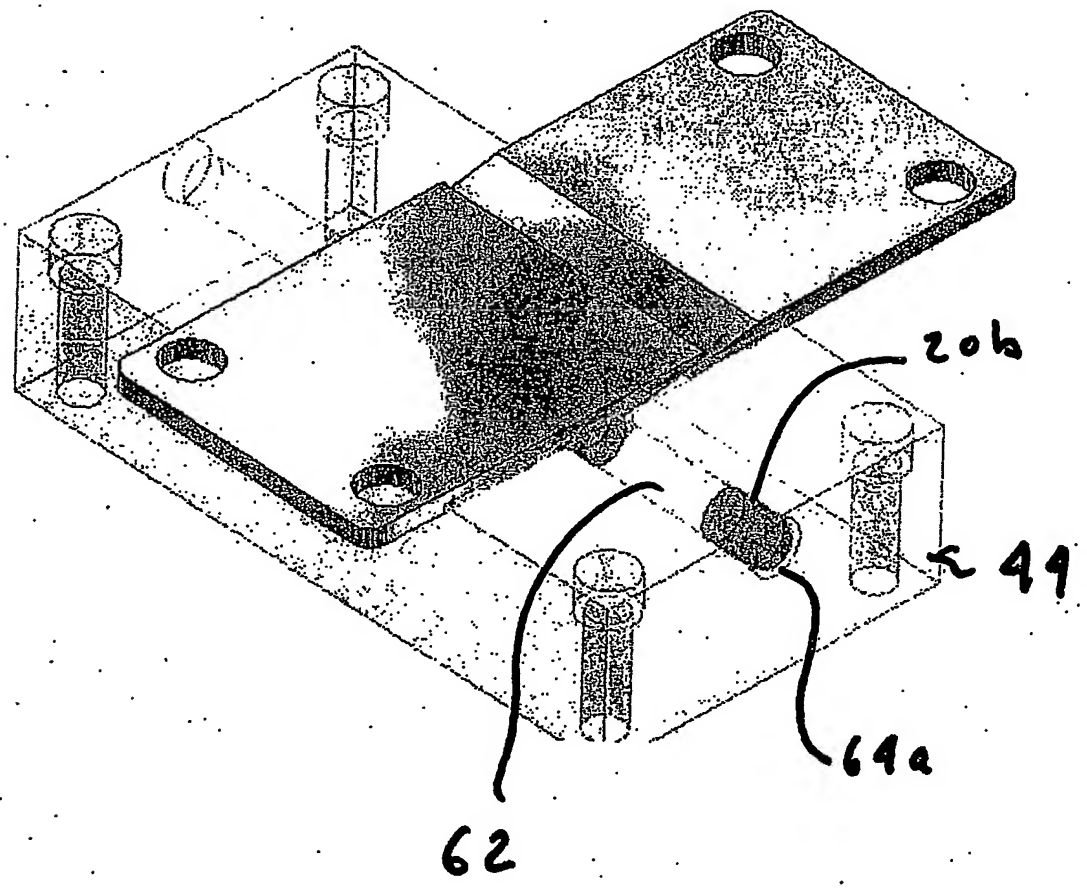

FIG 11A

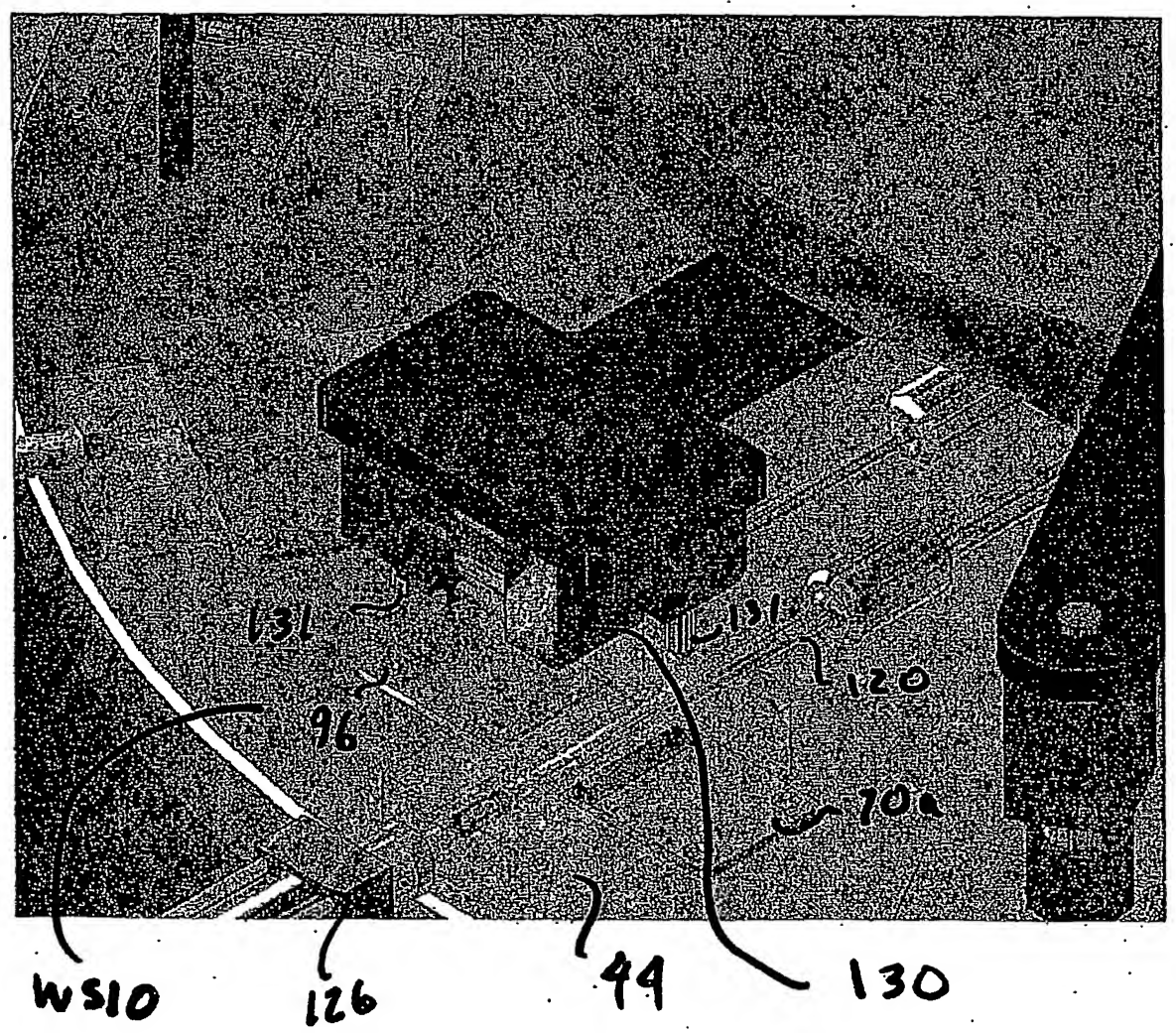

FIG 12

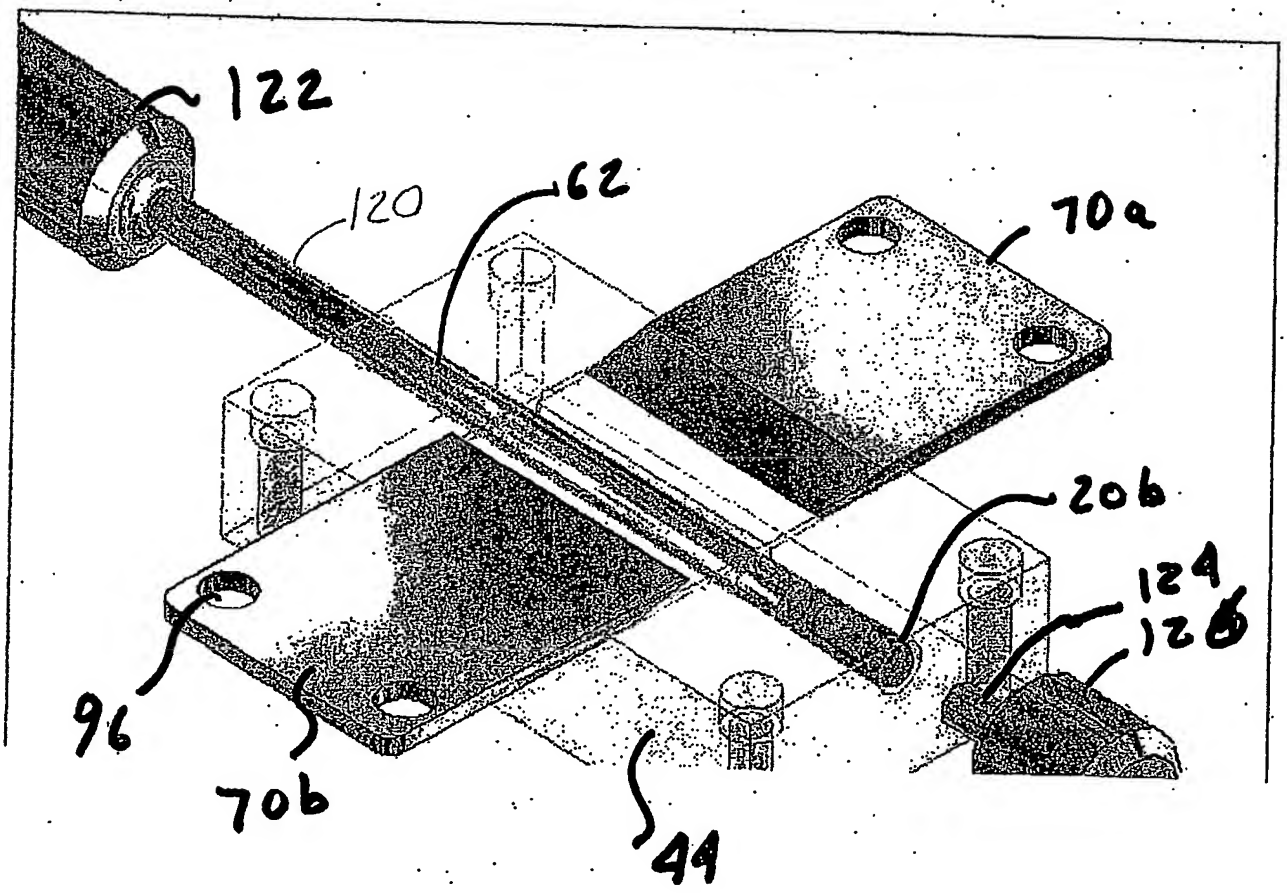

FIG 12A

FIG 13

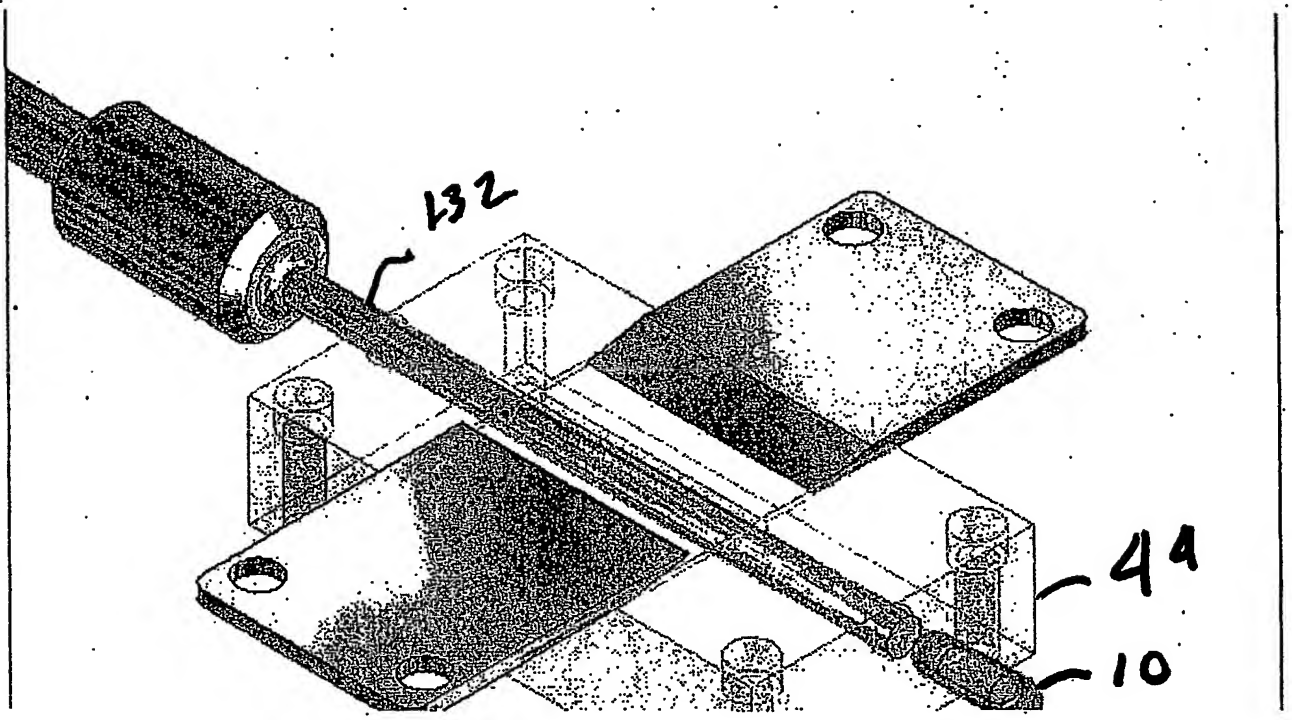

FIG 13A

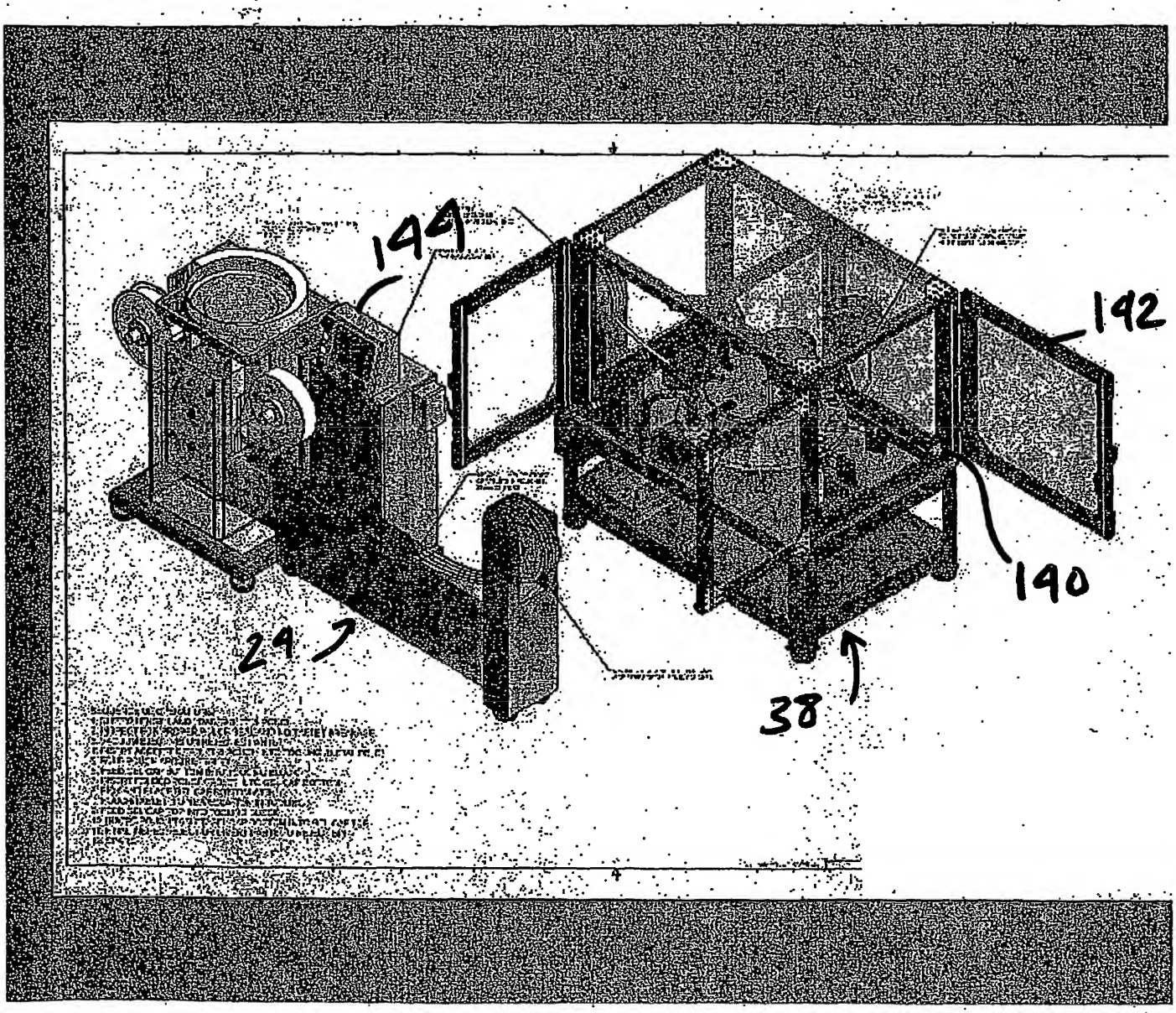

FIG 19

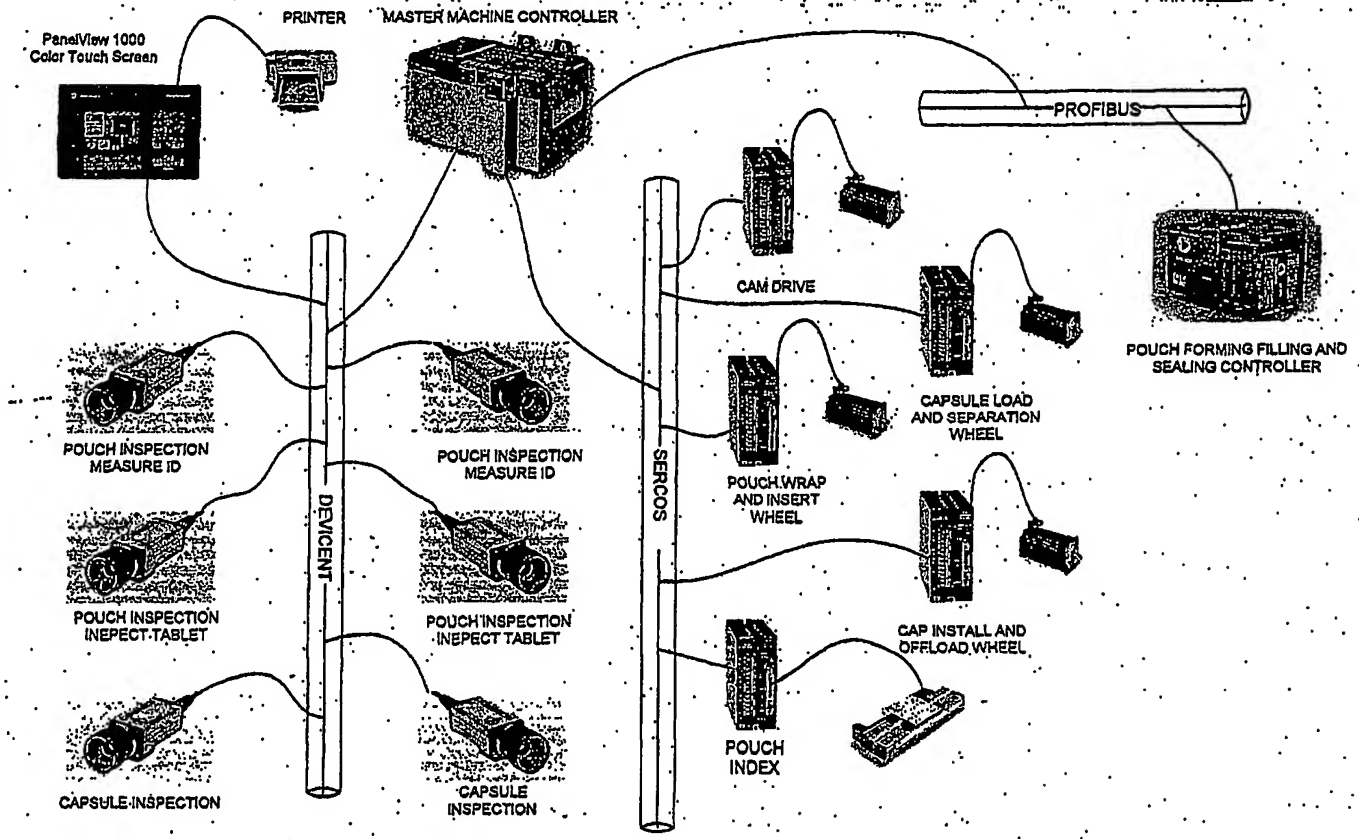

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Fig 15

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